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Elucidating the role of essential RNA secondary structural elements in dengue biology and their implication in dengue virulence

B. Mishra[1,*], H. Beesetti[2], A. Advait[1], S. Swaminathan[2], R. Aduri[1]

[1] *Birla Institute of Technology and Science - Pilani, K K Birla Goa campus, Goa, India*
[2] *Birla Institute of Technology and Science - Pilani, Hyderabad campus, Hyderabad, India*

Background: RNA-RNA interactions, central to many biological processes, are often mediated by various secondary structural elements of the RNA. In the context of single-stranded RNA viruses such as Dengue virus (DENV) and other flaviviruses, such RNA-RNA interactions may be the key to switching between translation and replication. DENV (serotypes 1-4) is the causative agent of Dengue fever (DF), Dengue hemorrhagic fever (DHF), and Dengue shock syndrome (DSS). Each of the DENV serotypes is further classified into several genotypes having varying degrees of pathogenicity and virulence. One of the conserved features of DENV and other flaviviruses is the presence of complementary sequences in the 5'- and 3'-untranslated regions (UTRs) that participate in long-range RNA-RNA interactions leading to the circularization of the genome. We hypothesized that the differences in secondary structures (and the corresponding three-dimensional orientation) of the 5' and 3' UTRs of the DENV RNA genome may underpin differences in virulence and pathogenicity of the different genotypes. Currently, there is no global scale analysis of DENV genomes correlating the RNA secondary structure with pathogenicity and virulence.

Methods & Materials: Towards this end, we have curated the NCBI database for full length genomes of DENV and classified them according to their respective genotypes. Using mFOLD, we derived the putative RNA secondary structures of the 5'- end of the RNA genome (encompassing the 5' UTR, the capsid hairpin (cHP), and the 5'- cyclization sequence (5' CS)) and the final 106 nucleotides of the 3'-UTR (comprising the 3'-SL and 3'-CS). Comparative analysis of the secondary structure elements of different genotypes was done using in-house software packages. We have also performed comparative analysis of these RNA structural elements across the serotypes.

Results: Our work has led to the observation of subtle but significant RNA secondary structure variations among not only the serotypes but within genotypes of a given serotype.

Conclusion: By carrying out an extensive global analysis of DENV genomic RNA secondary structure we were able to correlate serotype and genotype specific RNA secondary structural elements and their possible role in pathogenicity and virulence.

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Hepatitis A virus outbreak in a compound in Tshwane district, Gauteng, South Africa: October 2014-March 2015

M.R. Mphaka[1,*], T. Ntshiqa[1], L. Majake[2], C. Mugero[3], A. Maphele[4], M. Van Der Westhuizen[5], M. Moshime[5], R. Ncha[6], G.M. Ntshoe[6], T. Mkhencele[6]

[1] *South African Field Epidemiology Training Programme, National Institute for Communicable Diseases, Johannesburg, South Africa*
[2] *School of Health Systems and Public Health, Faculty of Health Sciences, University of Pretoria, Pretoria, South Africa*
[3] *National Department of Health, Pretoria, South Africa*
[4] *Tshwane Sub-district 2 health facility, Pretoria, South Africa*
[5] *Expanded Programme on Immunization/Communicable Disease Control/Outbreak Response , Pretoria, South Africa*
[6] *Division of Public Health Surveillance and Response, National Institute of Communicable Disease, Johannesburg, South Africa*

Background: Hepatitis A is a contagious viral infection caused by hepatitis A virus (HAV). It is strongly associated with socio-economic indicators such as access to clean water and sanitation. On 16 February 2015, the Tshwane Outbreak Response Unit (ORU) was notified by a laboratory of an increase in blood samples that tested positive for HAV IgM. On the same day Tshwane ORU team was assembled to conduct further investigations.

Methods & Materials: We interviewed residents of a privately owned residential compound using a structured questionnaire collecting demographic, clinical and history of exposure information. A probable case was defined as a person who had an epidemiological link to a confirmed case with an onset of two or more HAV symptoms. A confirmed case was a probable case with laboratory confirmation of HAV. Blood samples were collected from the available residents for HAV IgM antibodies. We conducted an environmental assessment and noted access to water in food preparation areas, sanitary facilities, and the drainage system. Samples were collected from taps and water storage containers for chemical analysis.

Results: Of the 46 households with ~ 80 residents, 42 were interviewed. The median age was 24 years: range of 6-55 years. We collected 46 blood samples: 12 (26%) tested positive for HAV IgM. Among the 12 confirmed cases, HAV infection was equally distributed across both genders and 50% (n=6) were <15 years. There were three probable cases, including one food handler who prepared food in a communal kitchen along with four other women. There was no running water in the kitchen. Water access was restricted. Buckets were used for storage in the houses, flushing toilets and portable basins used to wash hands without soap. The drainage system was poor: sewage pipes leaked and toilets drained